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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/060,188	04/14/1998	DOMINIC P. BEHAN		9333

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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/060,188	BEHAN ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,40 and 45-74* is/are pending in the application.

4a) Of the above claim(s) *71-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,40 and 45-74* is/are rejected.

7)☒ Claim(s) *64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/10/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on /y/z has been entered.

Status of Application, Amendments and/or Claims

The amendment of 7/10/06 has been entered in full. Claims 69 and 70 are amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 34, 40 and 45-74 are under consideration in the instant application.

Specification

The disclosure is objected to because of the following informalities:

(1) The title of the invention contains the word "identifying" misspelled as "indentifying".

(2) The title of the invention is not descriptive because it is broadly directed to a method for identifying modulators of "cell surface membrane receptors", yet the claims are more narrowly limited to methods of using G-protein coupled receptors. A new title is required that is clearly indicative of the invention to which the claims are directed.

Appropriate correction is required.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (1/10/2006).

The rejection of claims 34, 40 and 45-70 under 35 U.S.C. § 112, first paragraph at pg 5-12 for failing to provide enablement is *withdrawn in part*. Specifically, the parts of the enablement rejection that are directed to constitutive activation of orphan GPCRs, and correlation of orphan receptors with physiological function based on tissue expression are *withdrawn* in view of Applicants' amendments to the claims and Applicants' persuasive arguments at pg 11 of the 7/10/06 response. However, the enablement rejection of claims 34, 40 and 45-70 is *maintained* based on the lack of enablement associated with a lack of utility (see below).

The rejection of claims 40, 53, 55, 56, 58, 60, 68 and 70 under 35 U.S.C. § 102(e) is *withdrawn* in view of Applicants' amendment to the claims and Applicants' persuasive arguments at pg 12-15 of the 7/10/06 response.

Duplicate claims

(1) Applicants are advised that should claim 63 be found allowable, claim 65 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Each of claims 63 and 65 recites, "The method of claim 69 wherein said mammalian tissue source is a human tissue source."

(2) Applicants are further advised that should claim 64 be found allowable, claim 66 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

Each of claims 64 and 66 recites, "The method of claim 70 wherein said mammalian tissue source is a human tissue source."

Claim Objections

Claim 64 is objected to because of the following informalities:

(1) Claim 64 contains an extra space between the last word ("source") and the concluding period.

Appropriate correction is required.

Claim Rejections - 35 USC § 101, utility

Claims 34, 40, 45-70 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

This rejection was set forth previously at pg 3-5 of the 1/10/2006 Office Action. In an interview on 7/5/2006, the Examiner indicated that current amendments to the claims would result in withdrawal of the utility rejection under 35 U.S.C. § 101, utility. However, on further consideration it is necessary to maintain this rejection for the reasons set forth herein. Applicants' arguments presented in the 7/10/06 response have been fully considered, but are not found to be persuasive.

Applicants argue (pg 8-10) that the totality of the evidence demonstrates a specific, substantial and credible utility for the claimed invention, and that the Office has not provided evidence to support a *prima facie* case that a person of ordinary skill in the art would consider not consider the utility to be asserted by Applicants to be specific and substantial. Applicants submit that the specification and Watson Declaration clearly indicate that the skilled artisan at the time of filing could use expression data for a given GPCR to correlate the receptor to an associated disease or disorder. Applicants point to the Watson Declaration as teaching that a receptor's location (cell or tissue type) is more important to understanding the function of the receptor than identification of the receptor's ligand. Applicants assert that the Watson declaration shows that the GPCRs 19AJ, 19Y, 18A and 18AI have been correlated with certain diseases and disorders via their expression data. Applicants argue that the Office must accept Dr. Watson's

comments because the Office has not provided any factual evidence to show that one skilled in the art would doubt these comments. Applicants argue that the correlation between an orphan GPCR and a disease or disorder provides utility for any ligand identified by the instant claims.

Applicants' arguments, and the Watson Declaration, have been fully considered, but are not found to be persuasive. The orphan GPCRs described by Watson do not appear to be described in the instant specification at the time of filing and are therefore not relevant to the utility of the claims at the time of filing of the instant application. Furthermore, in each of the examples provided by Watson, further experimentation has been performed to reasonably correlate the orphan GPCR with a substantial utility. With respect to 19AJ, expression in islet cells did not necessarily indicate that the GPCR functioned in insulin secretion. In order to provide a reasonable correlation between the receptor function and insulin production it was necessary to demonstrate that insulin production was increased when the 19AJ GPCR was introduced into insulin producing cells. With respect to 18F, further experimentation was done to correlate reduction of expression with rapid loss of body weight. With respect to 19Y, 18A, and 18AI, the asserted utility is based on differential expression in tumors, which is different than determining function solely based on expression in normal tissues. 19BX may have a substantial utility as a marker of post-ischemic events; however this is based on correlation with a specific disease condition and not based solely on its expression in normal brain tissue.

Applicants' claims are directed to methods of screening using an endogenous GPCR that "has been associated with a disease or disorder" and "an endogenous ligand for said endogenous GPCR has not been identified" (claim 69 and dependent claims) or an endogenous constitutively active GPCR that "has been associated with a disease or disorder" and "an endogenous ligand for said endogenous GPCR has not been identified" (claim 70 and dependent claims). Each method of screening requires an orphan GPCR that has been associated with a disease or disorder. However, each claimed method lacks specific and substantial utility because the orphan GPCRs to be used are associated with an *unspecified* disease or disorder. As set forth in the Revised

Interim Utility Guidelines Training Materials (available at www.uspto.gov/web/offices/pac/utility/utilityguide.pdf), a specific utility is "a utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example...a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent of a disclosure of what condition can be diagnosed" (pg 5-6). Furthermore, a substantial utility must be "a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities...the following are examples of situations that require or constitute carrying out further research to identify or confirm a "real world" context of use and, therefore, do not define "substantial utilities": A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved. B. A method of treating an unspecified disease or condition. C. A method of assaying for or identifying a material that itself has no "specific and/or substantial utility"..." (pg 6). In the instant case, the instant specification, as filed, does not provide any examples of orphan GPCRs that were associated with a disease or disorder. The association of a known orphan GPCR with a disease or disorder constitutes "carrying out further research to identify or confirm a "real world" context of use".

In the case *In re Fisher* (76 USPQ2d 1225 (CA FC 2005)) the U.S. Court of Appeals Federal Circuit stated, "Patent application does not satisfy utility requirement of 35 U.S.C. §101 unless it discloses both "substantial" utility for claimed invention, in form of significant and presently available benefit to public, as well as "specific" utility, which is well-defined and particular benefit to public" (pg 1225) and "an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the "substantial" utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public" (pg 1230).

In summary, the proposed uses of the claimed invention rely on orphan GPCRs that are associated with unspecified diseases or disorders, and that require further

research to identify the nature of the specific diseases or disorders. Therefore, the instant application fails to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility.

Claim Rejections - 35 USC § 112, 1st paragraph

Claims 34, 40 and 45-70 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Applicants' response (7/10/06) does not contain any arguments specifically directed to the enablement rejection as it relates to the utility rejection. Therefore, the enablement rejection is maintained for the reasons described in the utility rejection set forth above.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 34, 40 and 45-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants address their arguments (7/10/06; pg 11-12) to two portions of the previous written description rejection, which was set forth at pg 12-14 of the 1/10/06 Office Action.

In the first section of their arguments ("Constitutive Activation"), Applicants argue that one of skill in the art would recognize that orphan GPCRs could be constitutively activated in any number of ways and thus Applicants were clearly in possession of the invention at the time of filing. Applicants point to the previous Office Action which indicated that several methods have been indicated as predictable.

This argument has been fully considered and is found persuasive. The Examiner considers the several specific predictable methods of constitutively activating GPCRs

(set forth previously; see the 1/10/06 Office Action) to provide support for the method in general.

In the second section of their arguments ("Correlation to a physiological function"), Applicants submit that rejection is obviated in view of the the amendments to the claims, which remove the language concerning correlation of the orphan GPCR with a physiological function.

This argument has been fully considered but is not found persuasive. The Examiner acknowledges that Applicants have removed the language concerning correlation of the orphan GPCR with a physiological function. However, Applicants have replaced this language with the recitation that "said endogenous GPCR has been associated with a disease or disorder" (in each of claims 69 and 70). However, each genus of GPCR (required to practice the method of the claims) recited in the claims lacks written description. The method of claim 69 requires an endogenous GPCR "wherein said endogenous GPCR has been associated with a disease" and "an endogenous ligand for said endogenous GPCR has not been identified". That is, the method requires an orphan GPCR that has been associated with a disease. However, the specification as originally filed does not provide a description of any orphan GPCR that meets the description of the GPCR required by claim 69 or 70. The specification provides examples of orphan GPCRs, such as GPR3, GPR6 and GPR12 (pg 76), but does not teach a disease or disorder that is associated with any of these orphan GPCRs.

With respect to independent claim 70, the claimed method requires an endogenous constitutively active GPCR "wherein said endogenous GPCR has been associated with a disease" and "an endogenous ligand for said endogenous GPCR has not been identified". That is, the method requires a constitutively active orphan GPCR that has been associated with a disease. However, the specification as originally filed does not describe any examples of endogenous constitutively active orphan GPCRs that have been associated with a disease or disorder. Applicants refer to a constitutively active GPCR that is associated with a Kaposi's sarcoma (pg 65). However, a ligand for this GPCR was known prior to Applicant's filing of the instant application on April 14,

1997. Specifically, Gershengorn (January 1997) discloses that IL-8 can to this GPCR (see Figure 1 of Gershengorn et al. 1997. Nature. 385(6614): 347-350). Therefore, this GPCR does not meet the requirement of the claims that an endogenous ligand has not been identified.

The written description requirement for a genus required for a claimed method may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information of any orphan GPCRs that are associated with a disease or disorder. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the nature of the orphan GPCRs required for the claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is

required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, the claims do not meet the written description provision of 35 U.S.C. §112, first paragraph. Applicants are reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see pg 1115).

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 63-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 63 and 65 each depend from claim 69, and each recites the limitation "said mammalian tissue source" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. In the 7/10/2006 amendments to the claims, the phrase "mammalian tissue source" was deleted from parent claim 69.

Claims 64 and 66 each depend from claim 70, and each recites the limitation "said mammalian tissue source" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. In the 7/10/2006 amendments to the claims, the phrase "mammalian tissue source" was deleted from parent claim 70.

Claim 67 depends from claim 69, and recites the limitation "said physiological function" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. In the 7/10/2006 amendments to the claims, the phrase "physiological function" was deleted from parent claim 69.

Claim 68 depends from claim 70, and recites the limitation "said physiological function" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. In the 7/10/2006 amendments to the claims, the phrase "physiological function" was deleted from parent claim 70.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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